

I. AN ISOMER OF THIAMIN

II. A DIRECT SYNTHESIS OF 4-HYDROXYQUINOLINES

BY

ROBERT HAROLD REITSEMA

A.B., Calvin College, 1942

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE
UNIVERSITY OF ILLINOIS, 1945

URBANA, ILLINOIS

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I. AN ISOMER OF THIAMIN

INTRODUCTION

Due to the difficulty of obtaining a properly substituted pyrimidine ring, one of the simplest isomers of thiamin had not been prepared. It was therefore of interest to synthesize that isomer in which the positions of the methyl and amine groups are reversed.

DISCUSSION OF RESULTS

The synthesis of this isomer required the preparation of 2-amino-4-methyl-5-aminomethyl- or bromomethylpyrimidine. The reduction of 2-amino-4-methyl-5-carbethoxypyrimidine by catalytic, chemical, or electrolytic methods was unsuccessful. Neither the amide nor the hydrazide could be formed under normal reaction conditions and conversion of these to the cyano or hydroxymethylpyrimidine could not be undertaken.

The synthesis of the desired pyrimidine was realized by the application of a typically aromatic reaction, a Rosenmund-von Braun reaction, to the pyrimidine ring. 2-Amino-4-methyl-5-bromopyrimidine was thus converted to 2-amino-4-methyl-5-cyanopyrimidine. The nitrile group was reduced catalytically to produce 2-amino-4-methyl-5-aminomethylpyrimidine. The corresponding 2-amino-4-methyl-5-thioformaminomethylpyrimidine was obtained in good yields. This pyrimidine was condensed with 3-aceto-3-bromopropyl acetate to yield 3-(2'-amino-4'-methyl-5'-pyrimidylmethyl)-4-methyl-5-(2-hydroxyethyl)-thiazolium bromide hydrobromide.

II. A DIRECT SYNTHESIS OF 4-HYDROXY- QUINOLINES

INTRODUCTION

4-Alkylamino-7-chloroquinolines have been found to be

more effective against malaria than either atabrine or quinine. The preparation of these drugs necessitated a useful synthesis of the parent compound 7-chloro-4-hydroxyquinoline. Although the most direct route to 4-hydroxyquinolines by cyclization of β -arylaminoacrylates had been abandoned by early workers, new techniques led to the decision to reinvestigate this reaction.

DISCUSSION OF RESULTS

By cyclizing methyl β -*m*-chloroanilinoacrylate in a large amount of inert solvent at about 250° the formation of the degradation product, *sym-bis-m*-chlorophenylurea, could be avoided. Under these conditions a 40 per cent yield of 7-chloro-4-hydroxyquinoline was obtained and its structure elucidated. In addition, small amounts of 5-chloro-4-hydroxyquinoline and a high melting isomer were obtained.

In a similar manner 4-hydroxyquinoline, and 7-chloro-4-hydroxy-3-methylquinoline were obtained. 7-Chloro-4-hydroxy-2-methylquinoline was produced by a Conrad-Limpach cyclization.

The product of a Mannich reaction on 7-chloro-4-hydroxyquinoline was characterized. 1-(3-Diethylamino-2-hydroxypropyl)-7-chloro-4-quinolinimine diphosphate was also prepared and found to be inactive toward malaria in ducks.

VITA

The author was born on June 25, 1920, in Grand Rapids, Michigan. He attended the public elementary schools of that city and Grand Rapids Christian High School. In the fall of 1938 he entered Calvin College and received the A. B. degree in June, 1942. He enrolled in the Graduate School of the University of Illinois in June, 1942, where he held a teaching assistantship until June, 1943, and a University Fellowship during the summer and fall terms of 1943. Since that time he has been a Special Research Assistant in Chemistry for the Office of Scientific Research and Development.



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